Kidney disease and obesity: evidence, challenges and future directions

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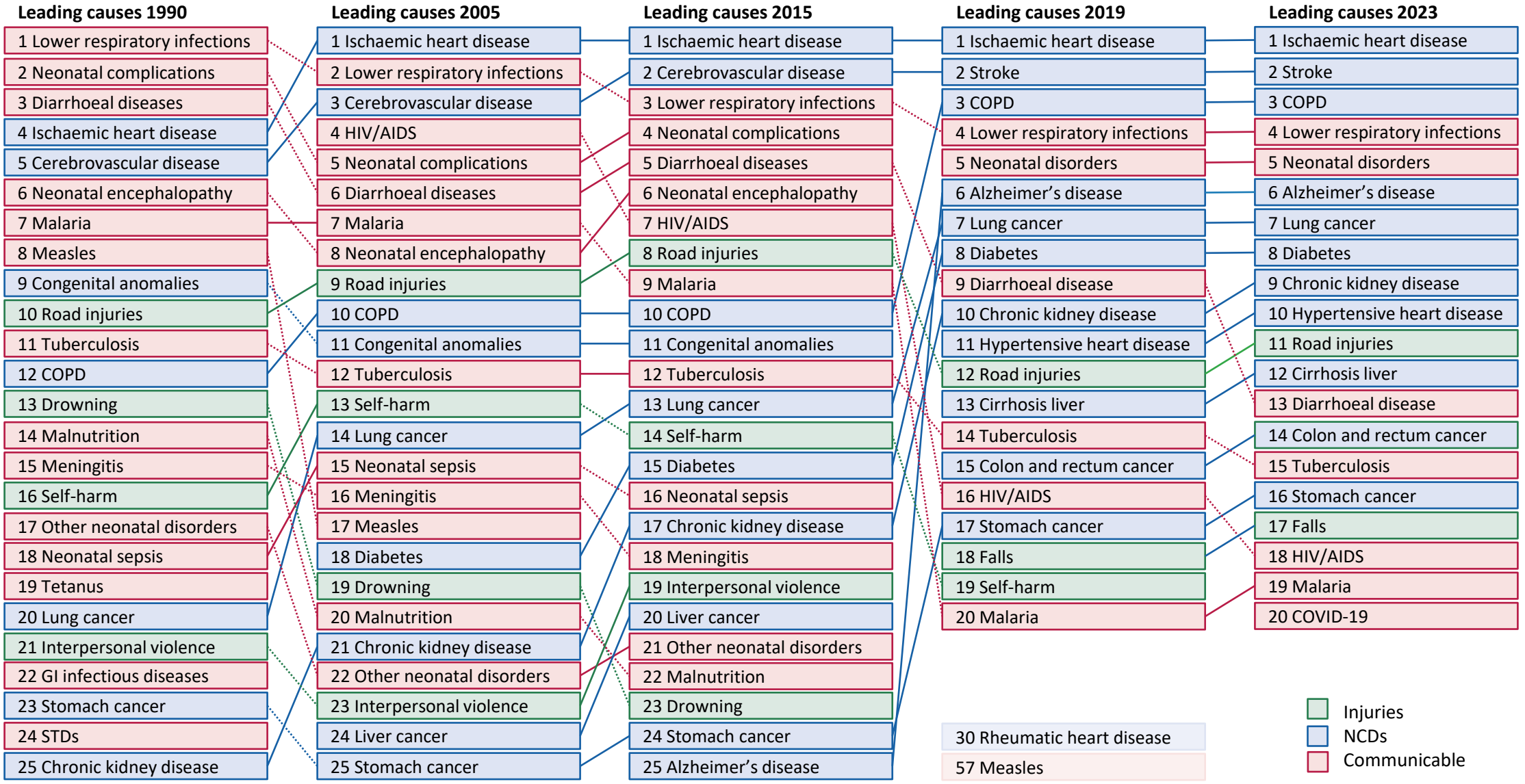
Mortality burden of CKD is rising

change in global number of deaths, 2005 - 2023



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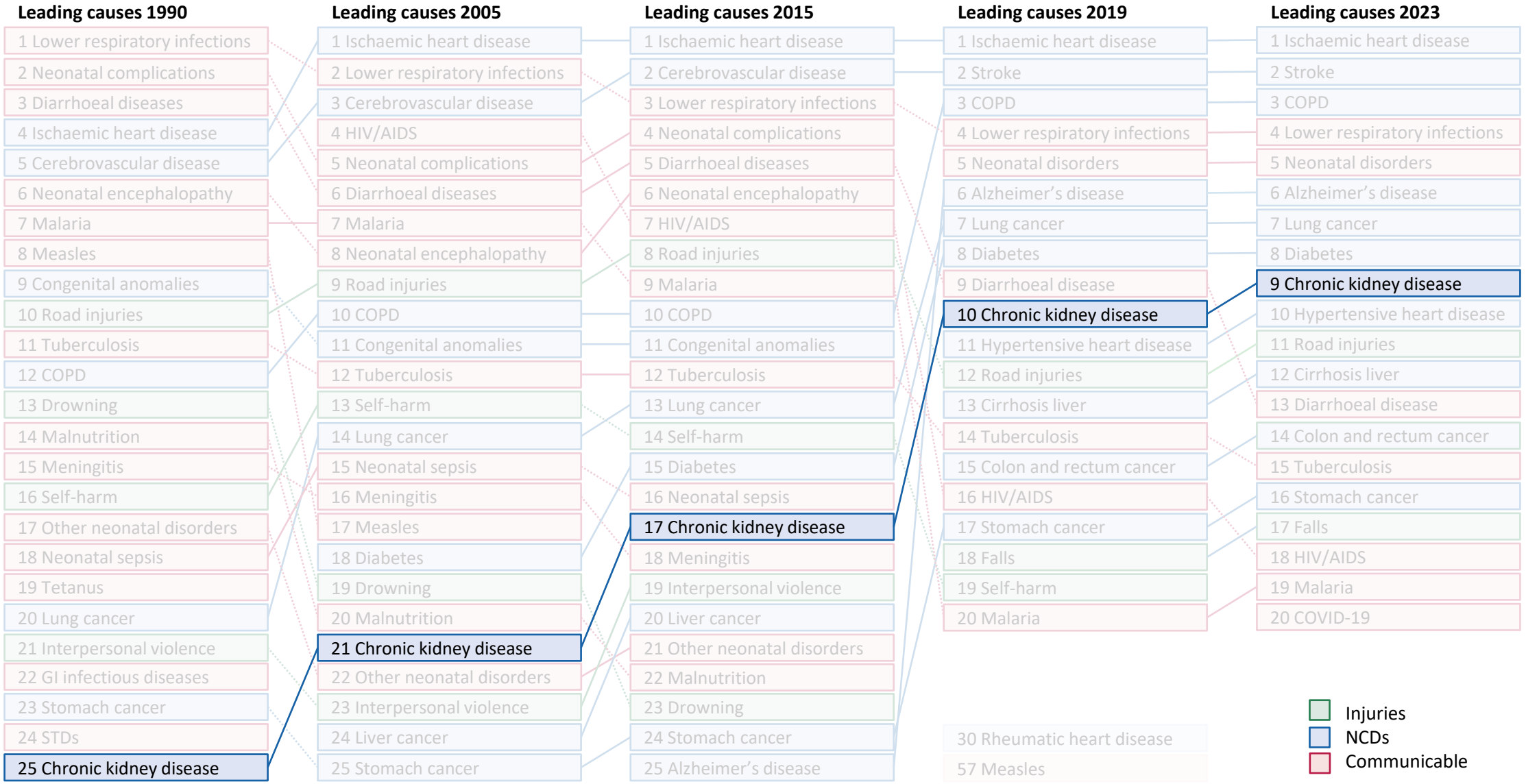
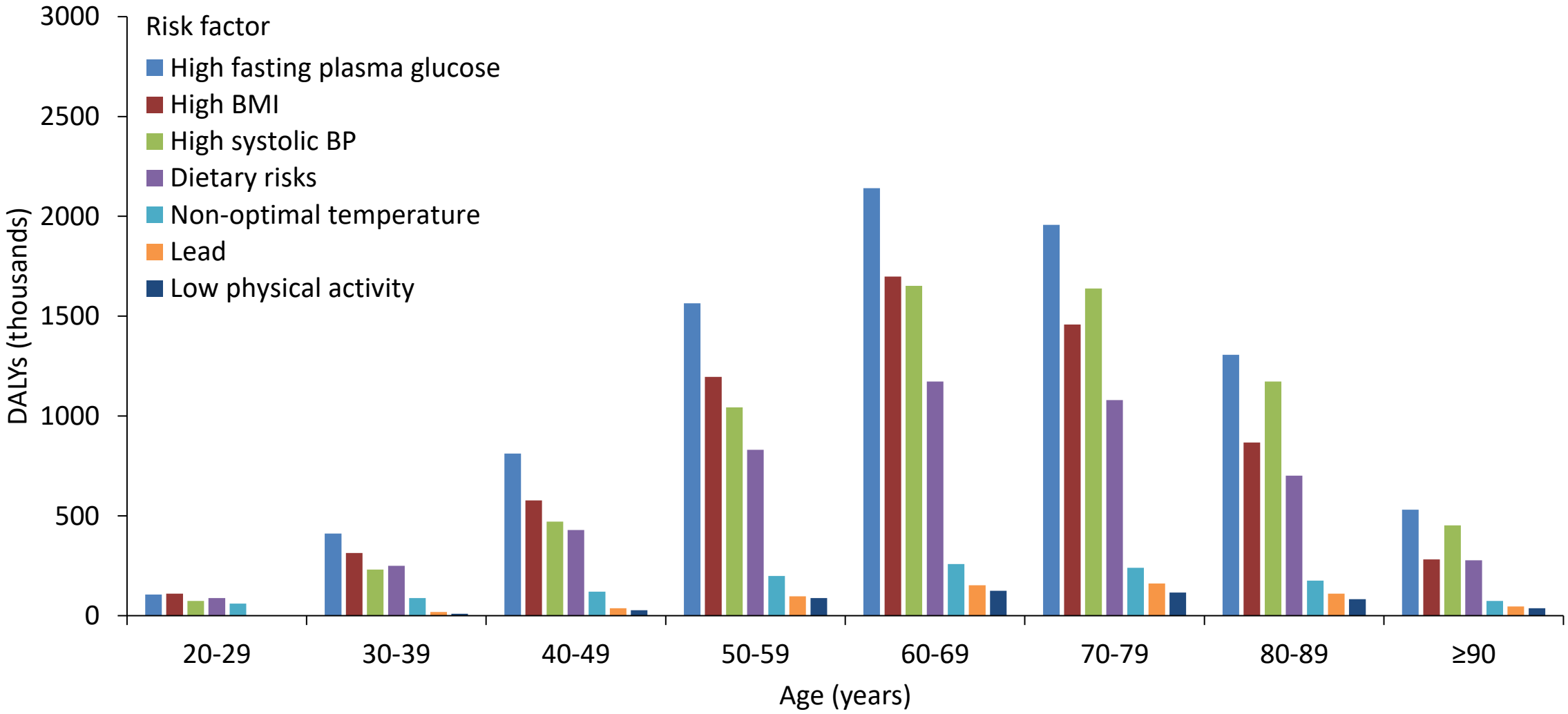
change in global number of deaths, 2005 - 2023



Risk factors attributed to the burden of CKD by age



GBD CKD Collaborators. Lancet 2025

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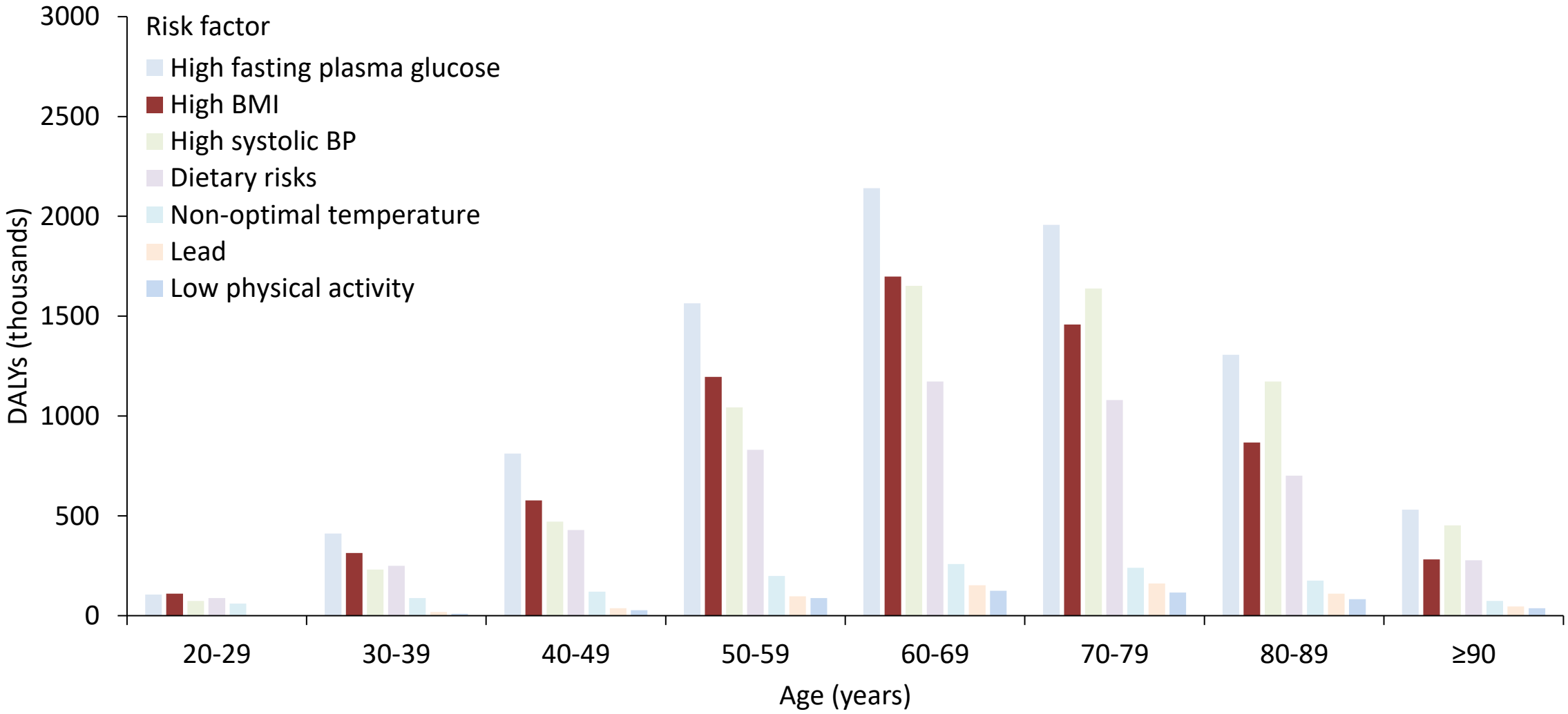
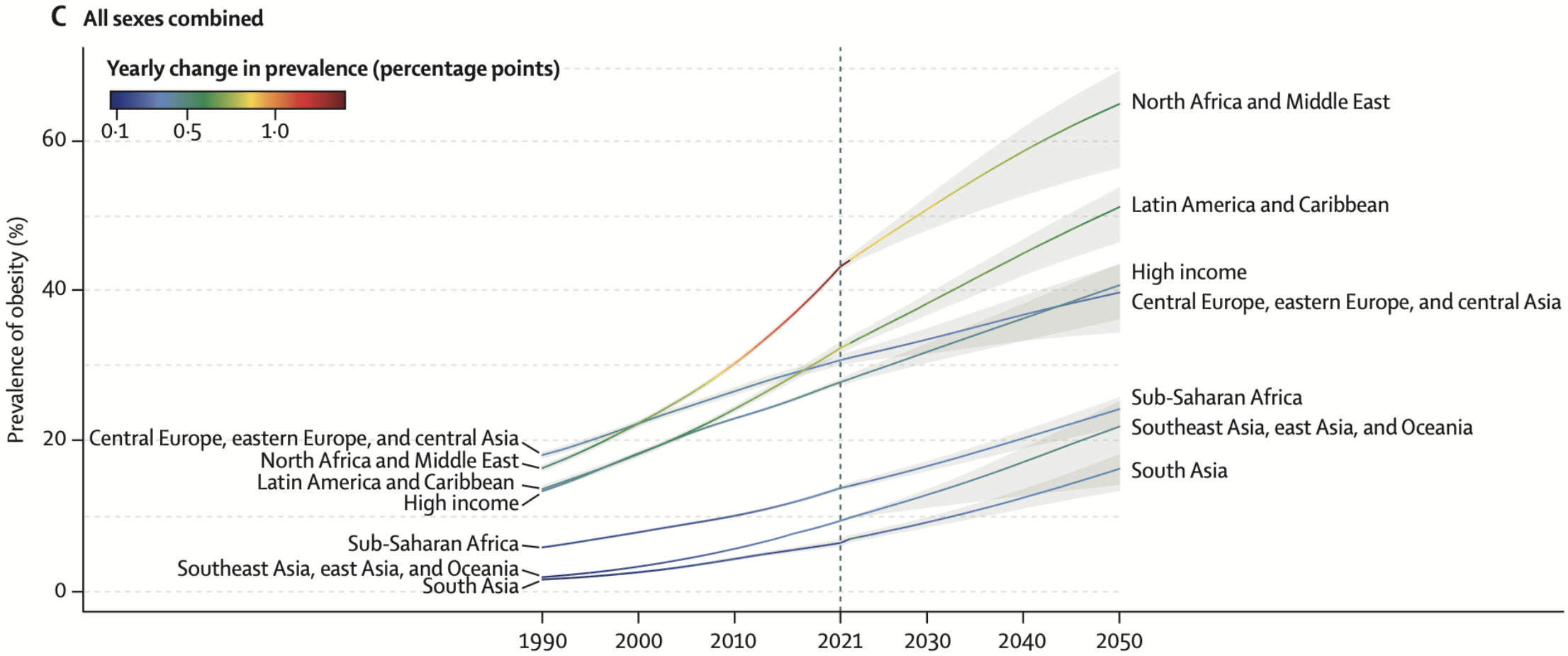


GBD CKD Collaborators. Lancet 2025

Prevalence of obesity is high and rising eveywhere

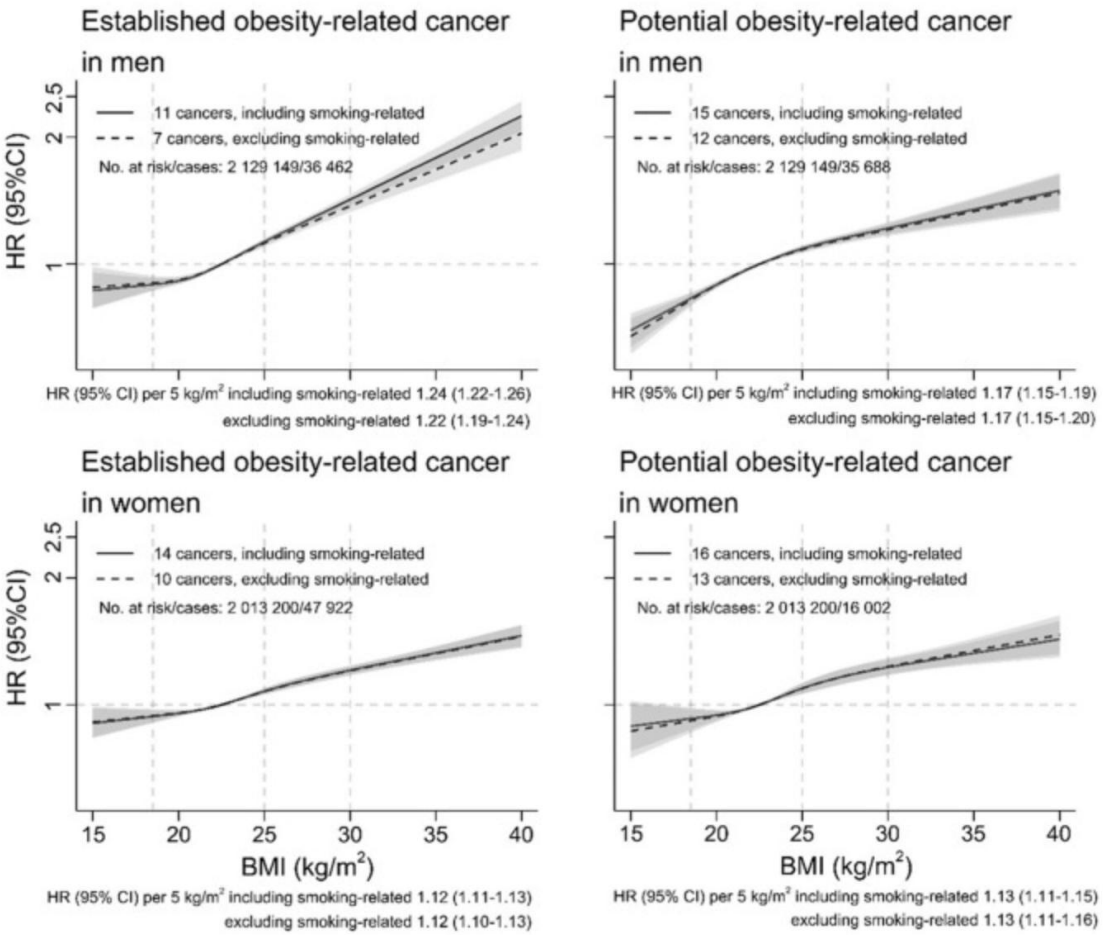


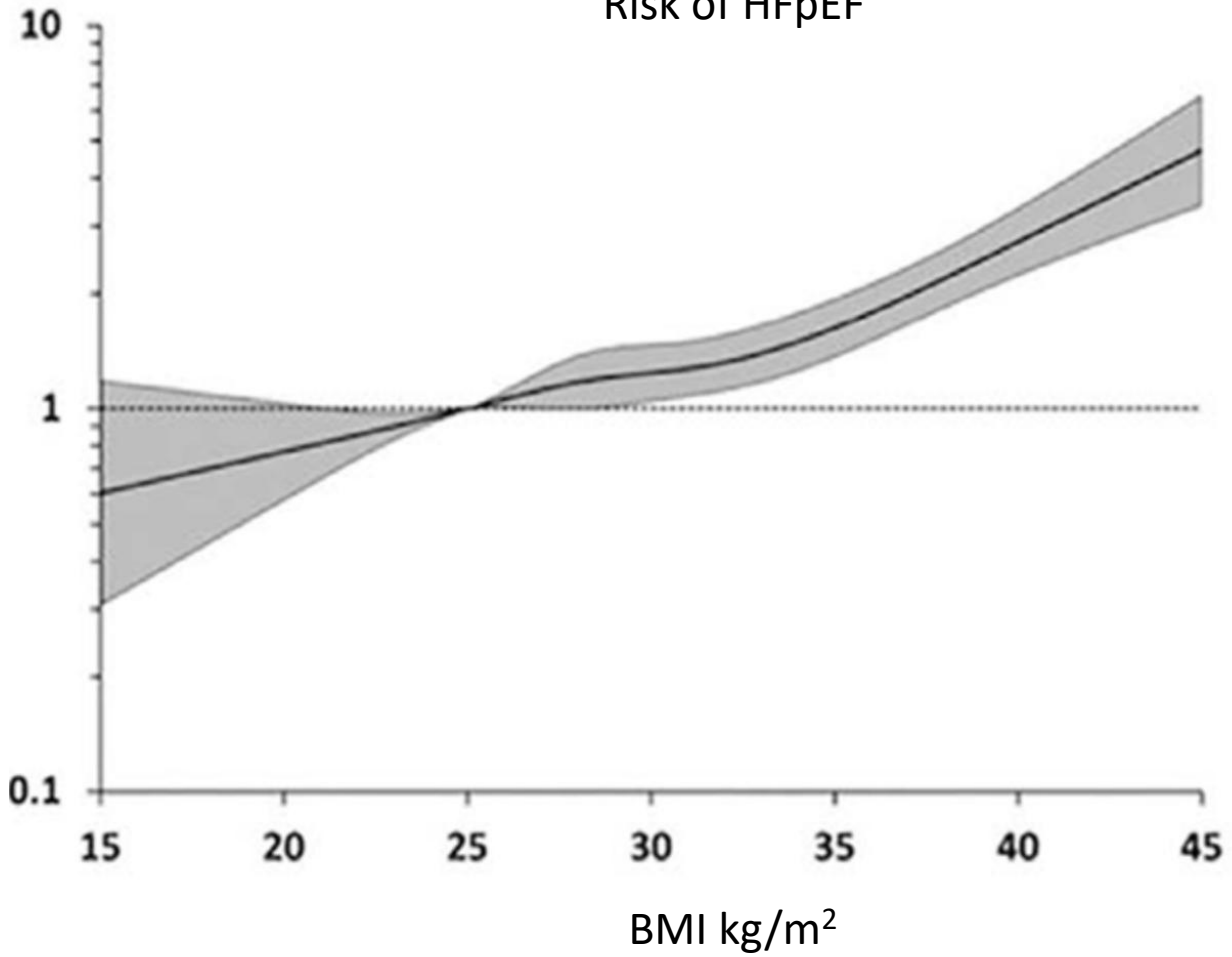
among adults aged 25y and older

GBD BMI Collaborators. Lancet 2021

The current paradigm

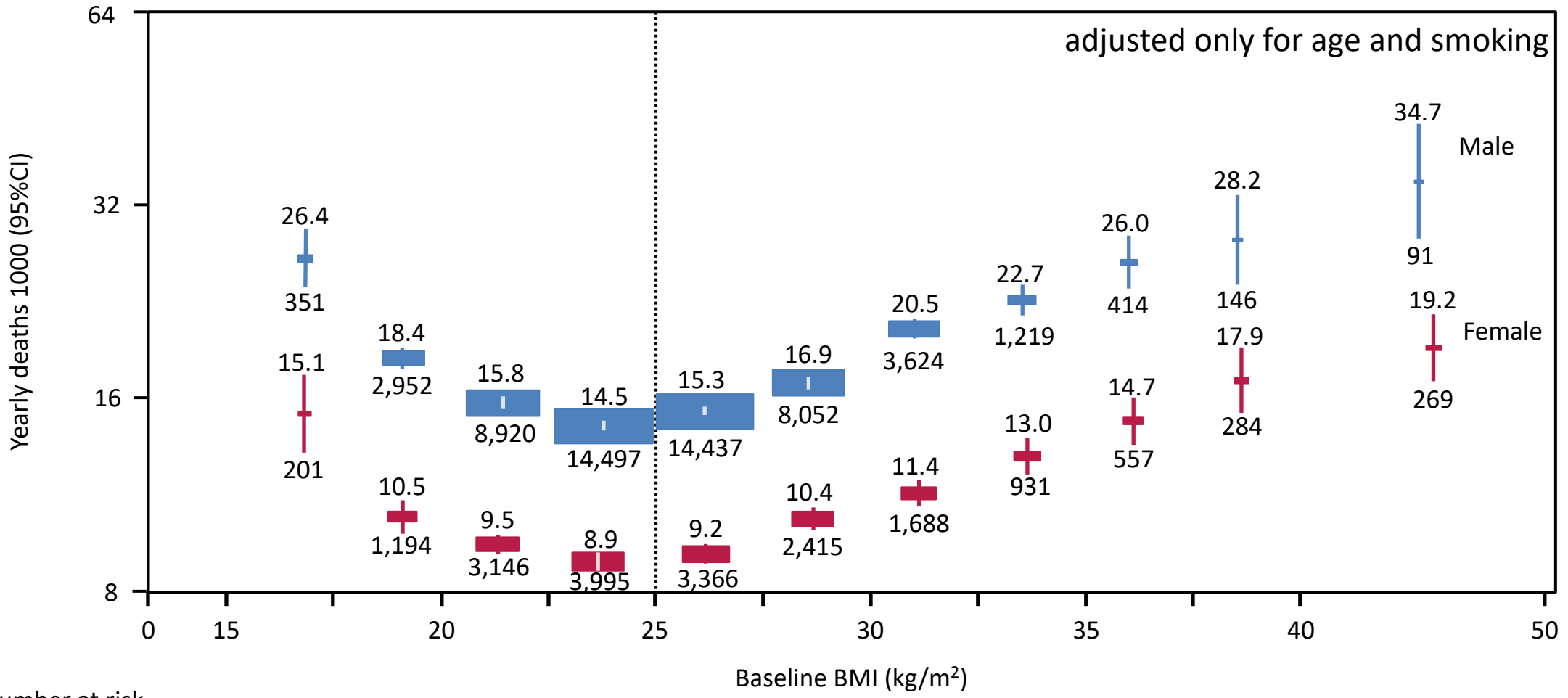
Higher BMI is associated with many adverse outcomes





Sun et al, Lancet Regional Health Europe 2024; Powell-Wiley et al, Circulation 2021

BMI is associated with mortality in the general population



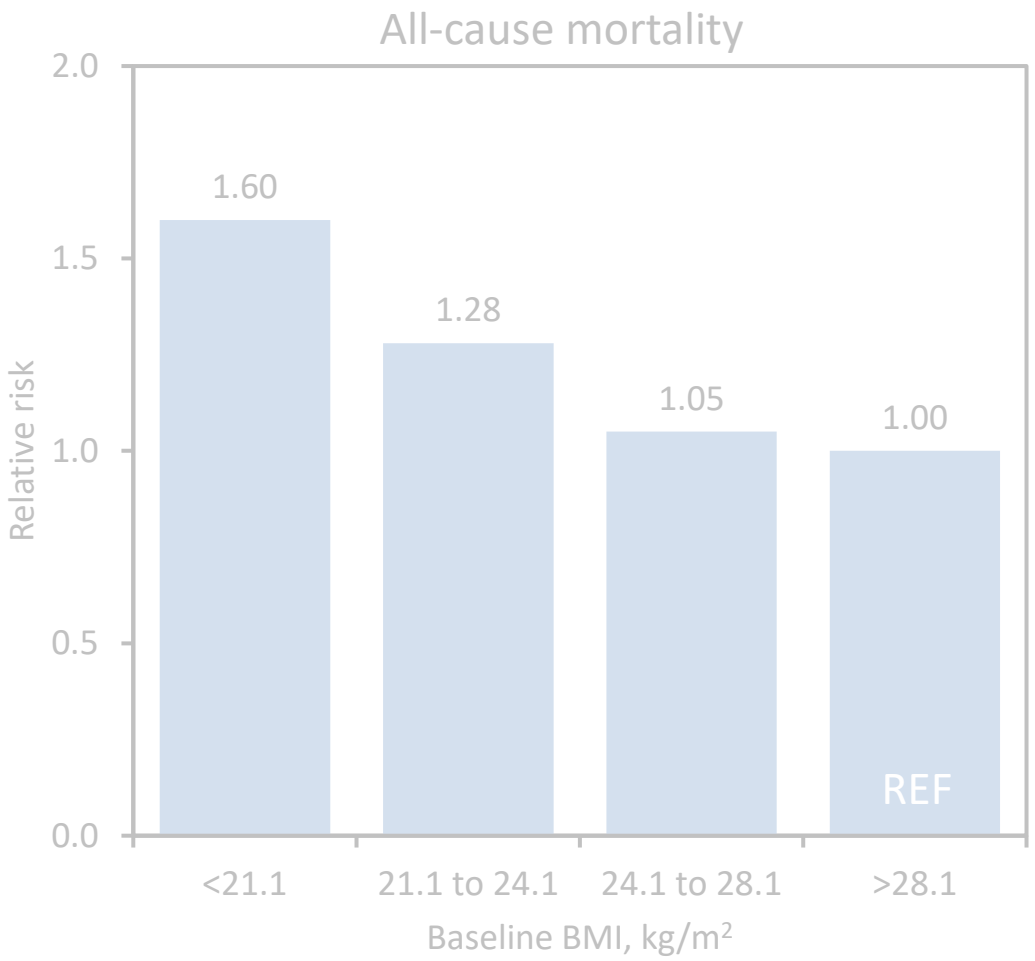
N=900,000
57 studies

Number at risk

Males	2,218	24,522	91,102	160,298	138,592	62,071	23,342	7,360	2,462	843	540
Females	3,295	34,617	88,348	86,970	57,023	30,824	18,372	9,366	5,100	2,821	2,738

Prospective Studies Collaboration, Lancet 2009

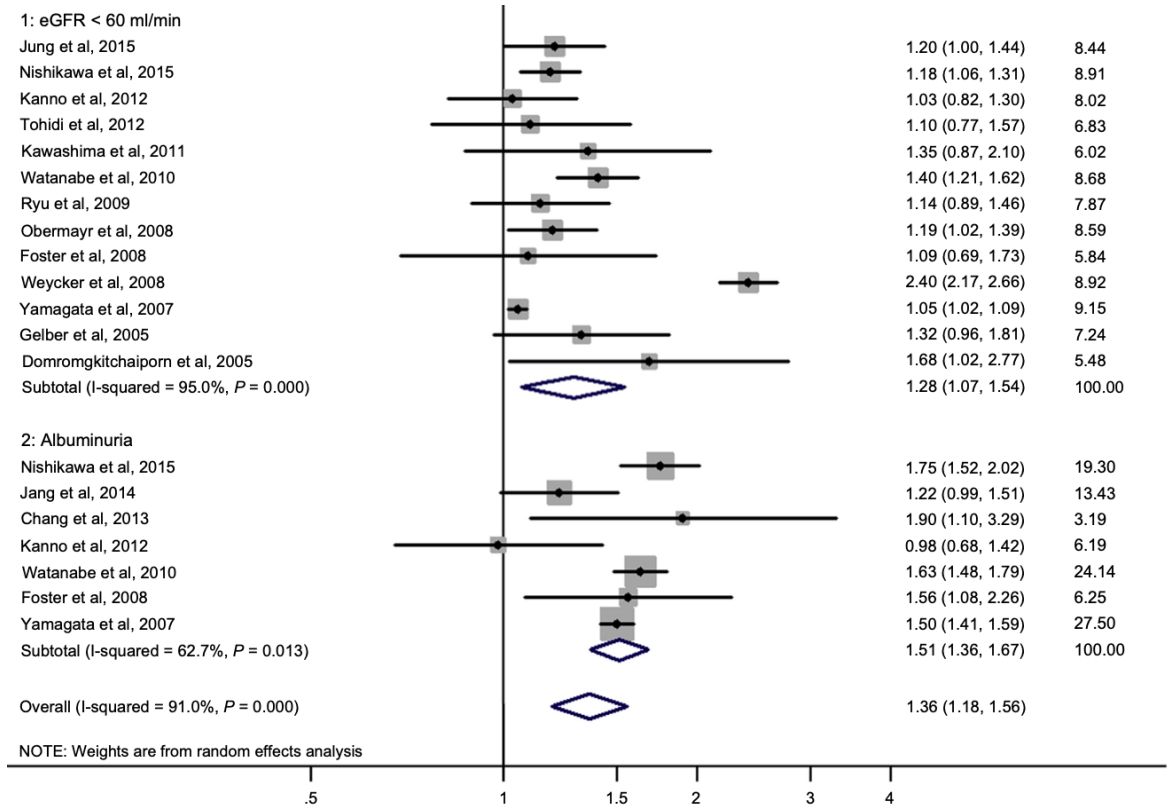
But not in hemodialysis patients

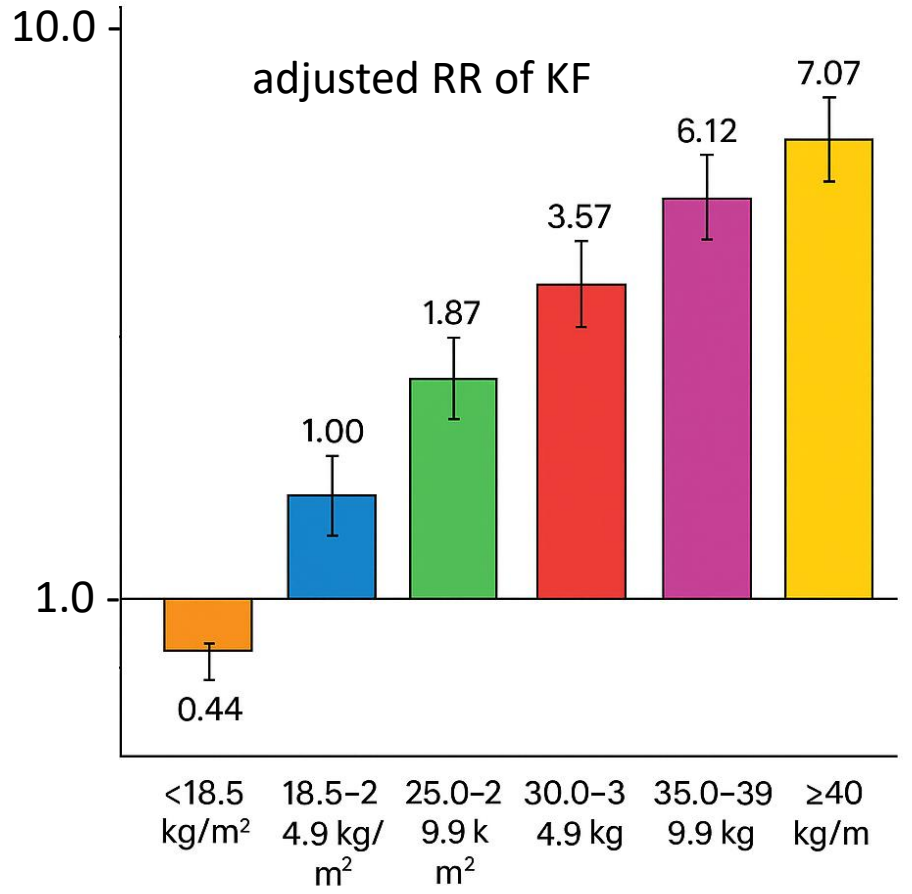


N=7719

Pifer, Kidney Int 2002; Kalantar-Zadeh Mayo Clin Proc 2010

However: higher BMI is associated with CKD and KF

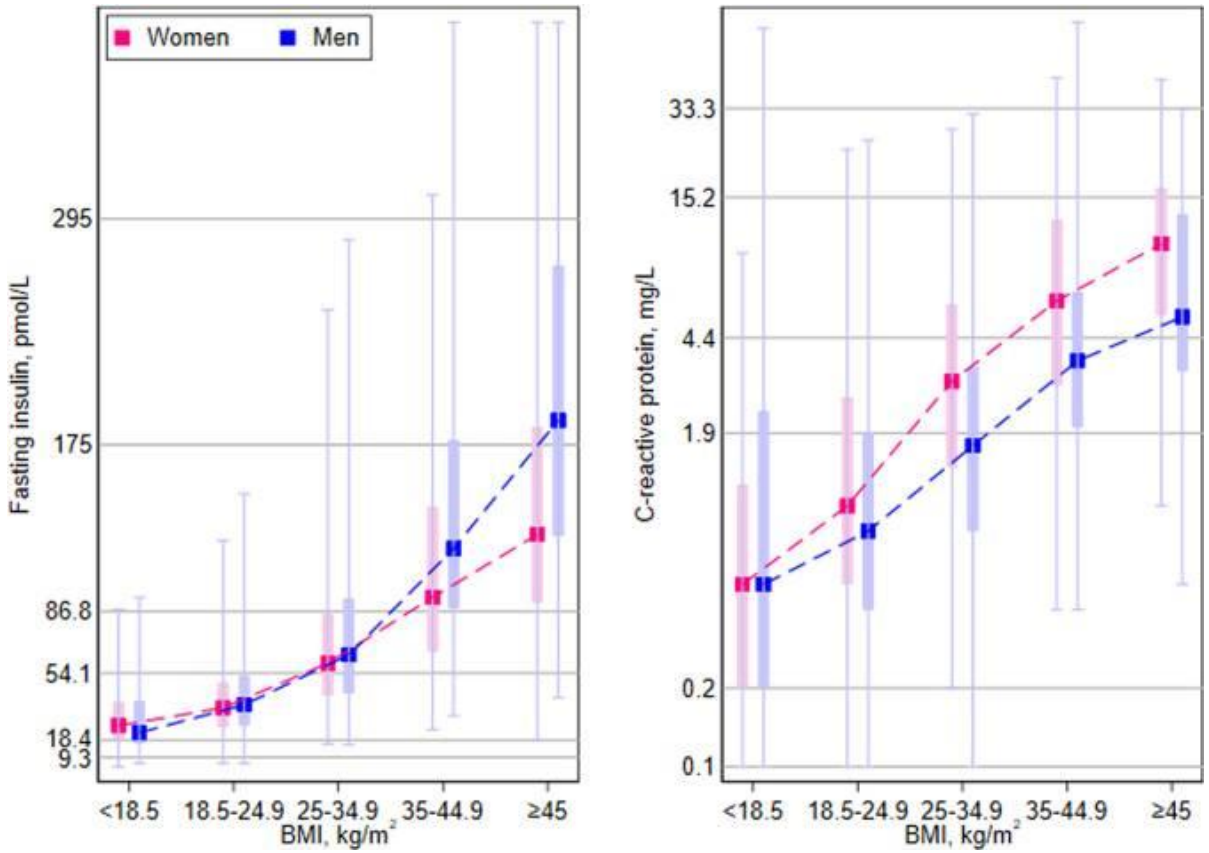




Adjusted for age, sex, race, education level, smoking status, history of myocardial infarction, serum cholesterol level, proteinuria, hematuria, and serum creatinine

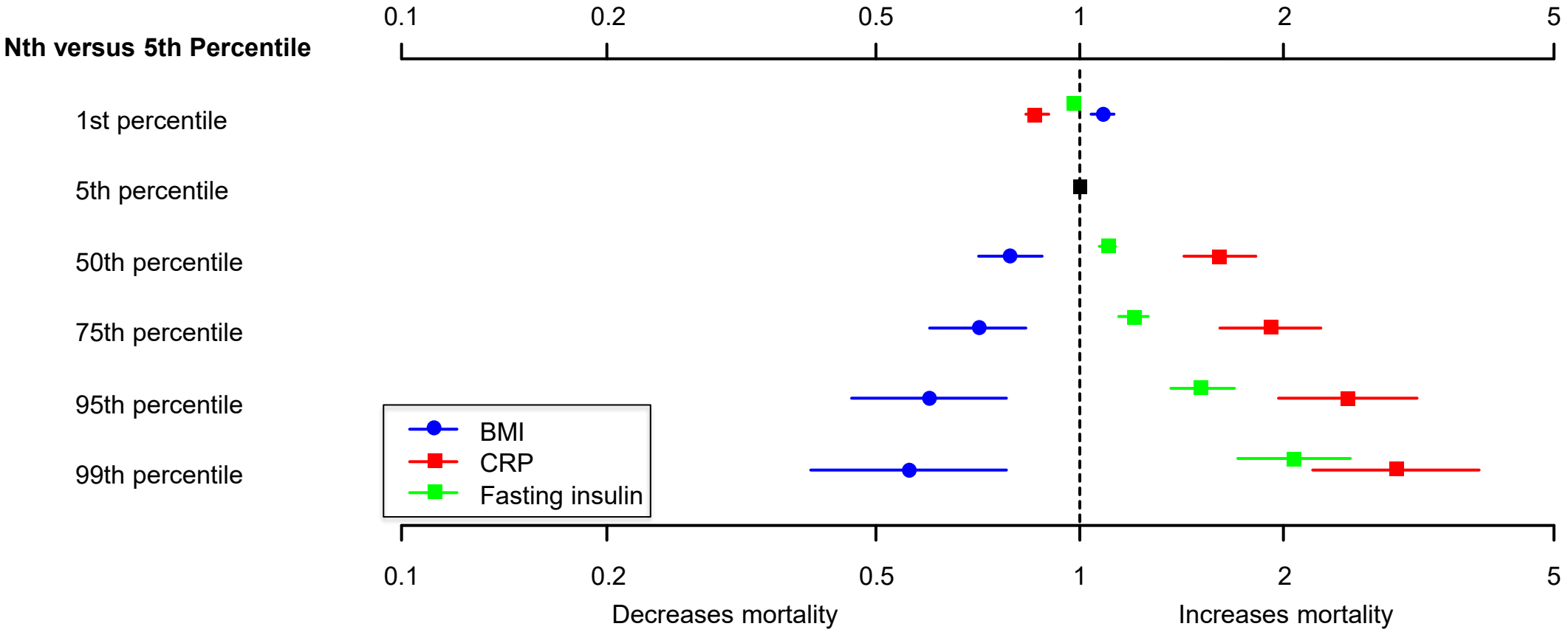
Garofalo C, Kidney Int 2017 Hsu CY, Ann Intern Med 2006

Higher BMI is correlated with levels of fasting insulin and c-reactive protein



Wiebe et al, Canadian Health Measures Survey

Obesity is actually “protective” after accounting for high CRP and hyperinsulinemia (NHANES)

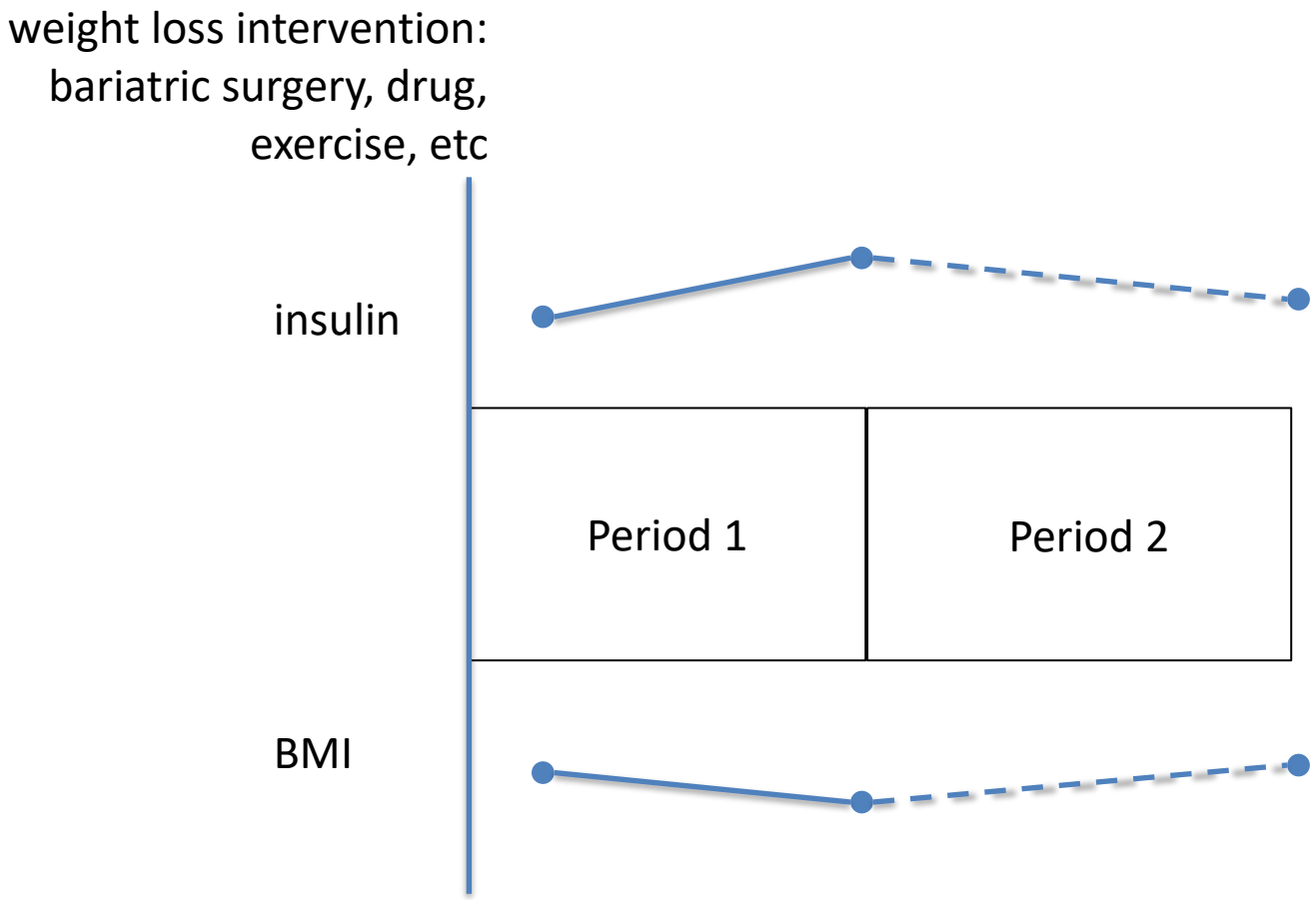


Wiebe et al, Int J Obes 2022

N=8280

Does obesity cause hyperinsulinemia?

findings from a systematic review of 60 studies suggest not…

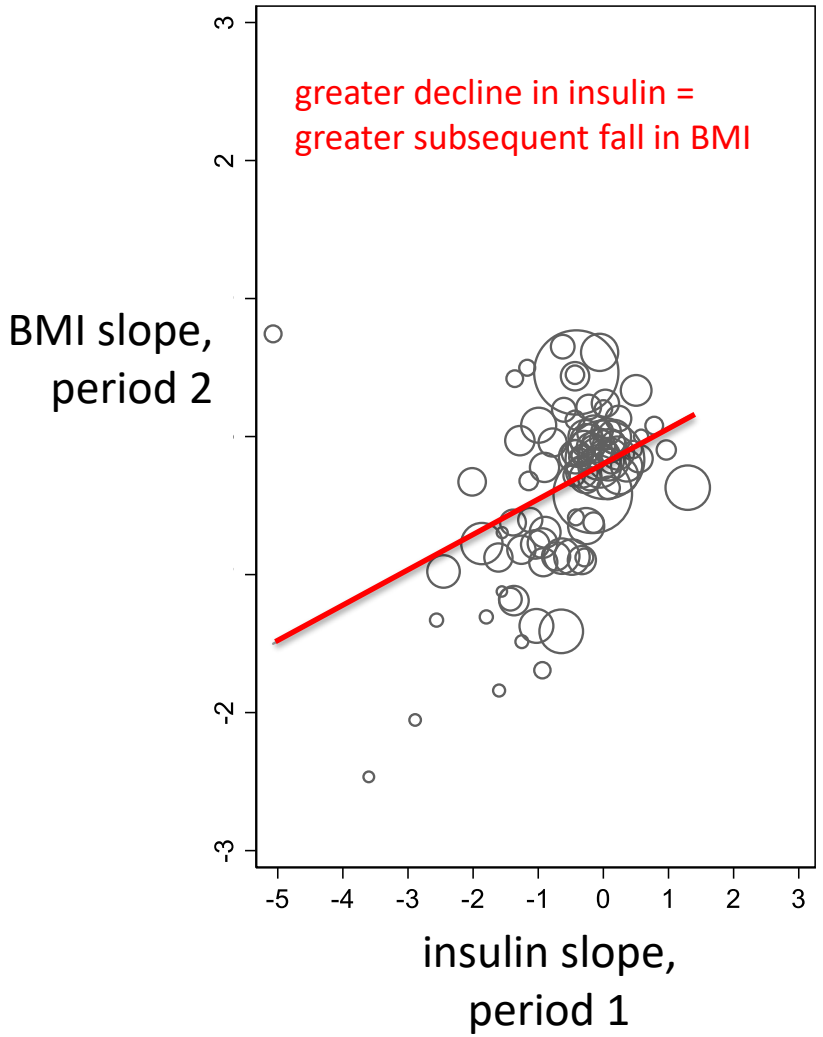


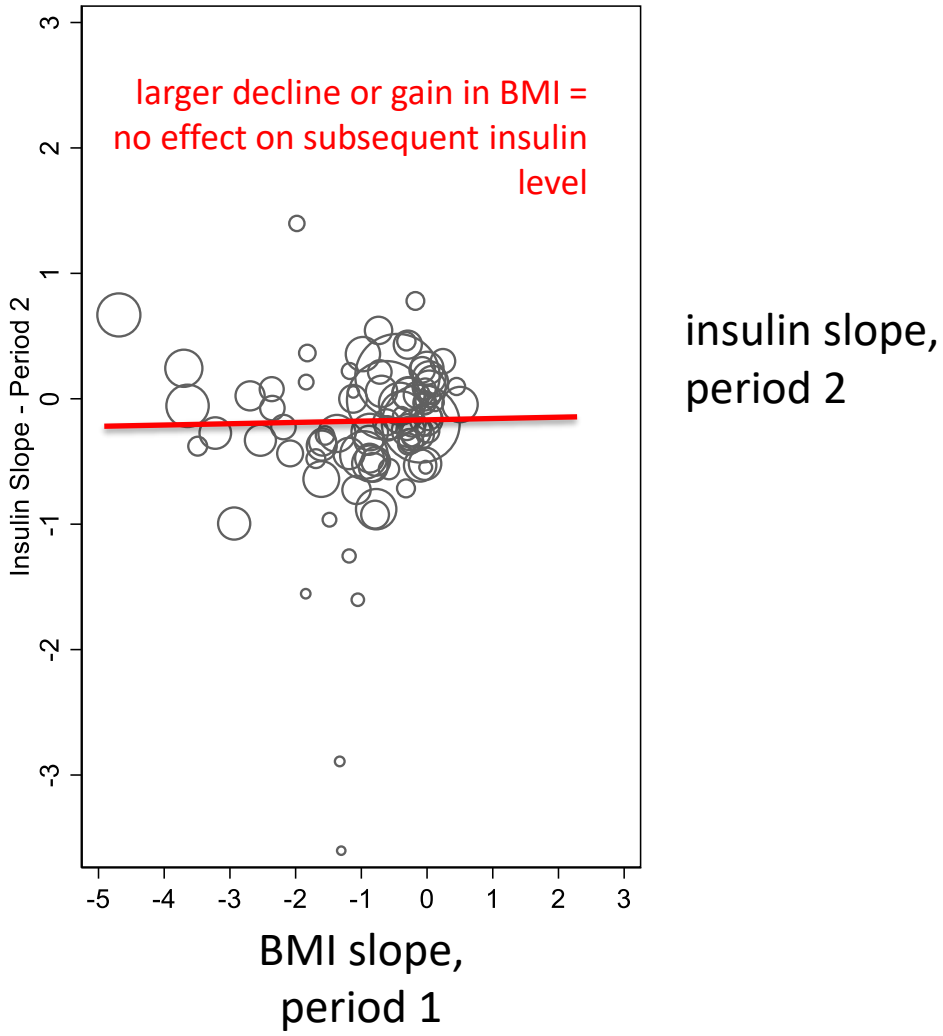
Which came first?

Did BMI rise in period 1, and then insulin in period 2?

Does obesity cause hyperinsulinemia?

findings from a systematic review of 60 studies suggest not…





Wiebe N. JAMA Network Open 2021

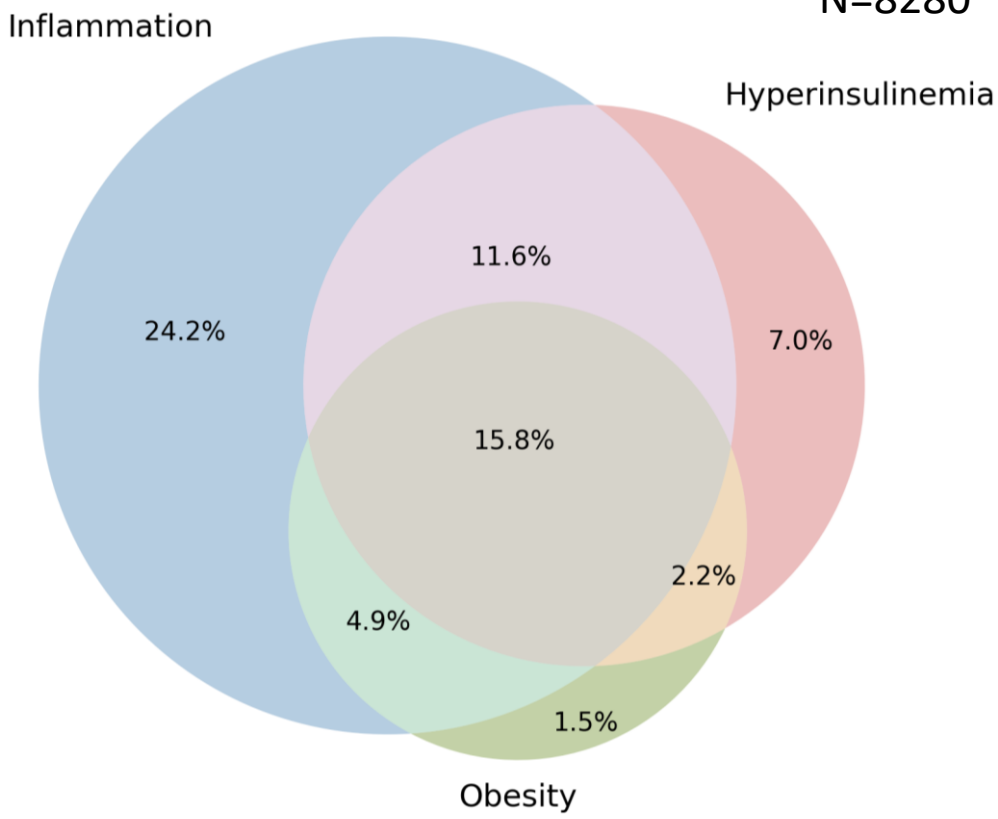
Higher BMI is correlated with levels of fasting insulin and c-reactive protein

Hyperinsulinemia: fasting insulin ≥75 pmol/l

Inflammation: hsCRP ≥1.1 mg/l

Obesity: BMI ≥30 kg/m^2

N=8280



42.8% of adults without obesity have either inflammation or hyperinsulinemia

11.6% of adults without obesity have both
15.8% of adults with obesity have both

Focusing only on people with obesity misses more than half of those with inflammation and hyperinsulinemia

32.8% of adults have none of these three

Wiebe et al, Canadian Health Measures Survey

Challenges

- Measuring GFR in people with obesity is difficult
- BMI is easy to measure (and judge) but insulin and CRP aren't
- Obesity is an extremely blunt phenotype
  - is it analogous to yellow fingers in cigarette smokers?
  - Is it analogous to smoke coming out of the window of a building?
- Obesity is common…so any "solution" has to work at scale
- Achieving weight loss is difficult
  - GLP1-ra seem effective but have side effects
  - will weight loss per se from GLP1-ra lead to clinical benefit ?

Implications

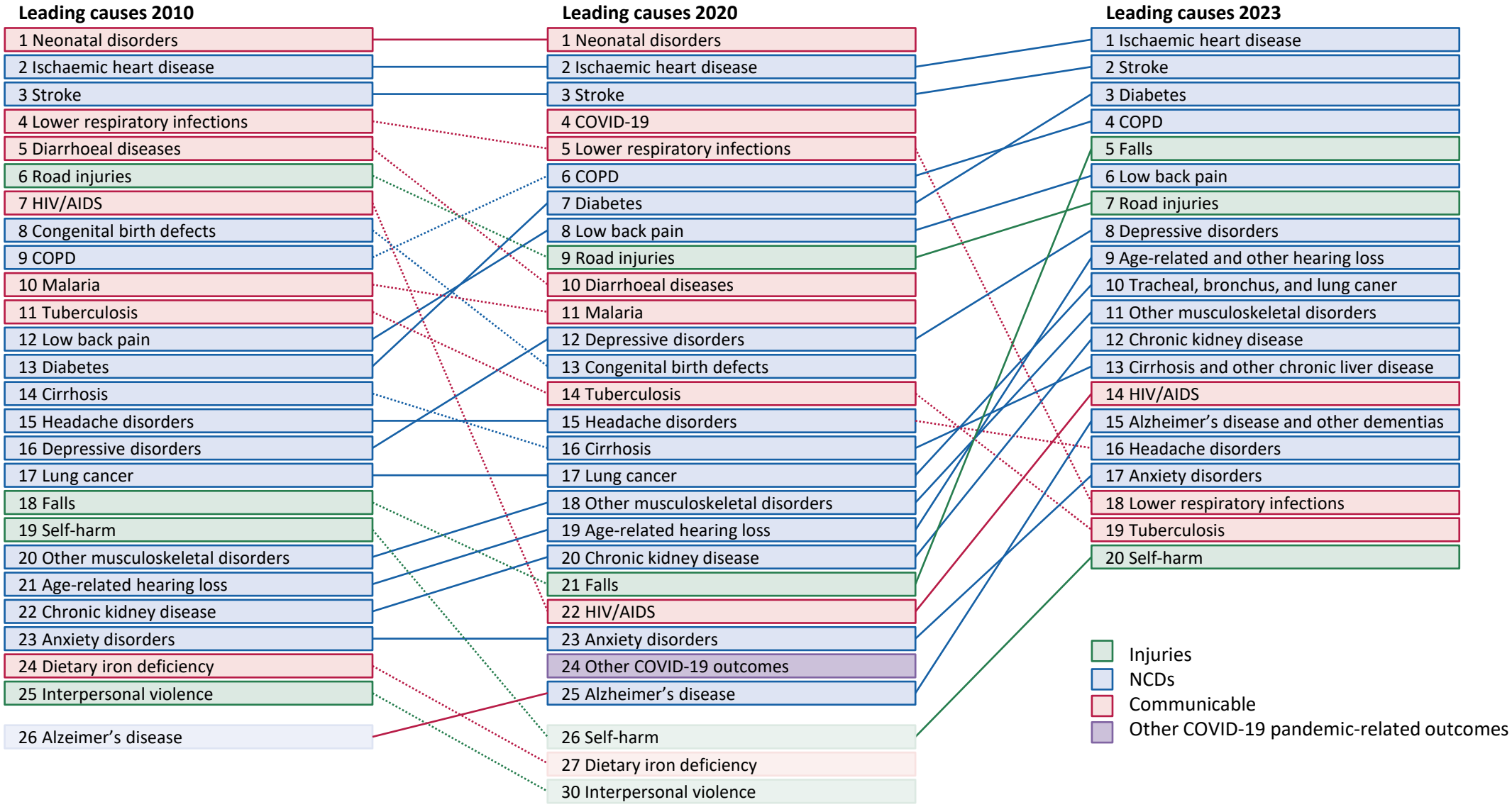
For public health:

- consider de-emphasizing obesity per se
- focus on what can be changed:
  - exercise
  - healthy diet
  - managing other kidney and CV risks

For research:

- more studies of insulin <-> CRP <-> obesity
- more studies on how to define obesity besides BMI
- more work on how to use GLP1-ra for those who are interested

CKD is an increasingly important cause of disability



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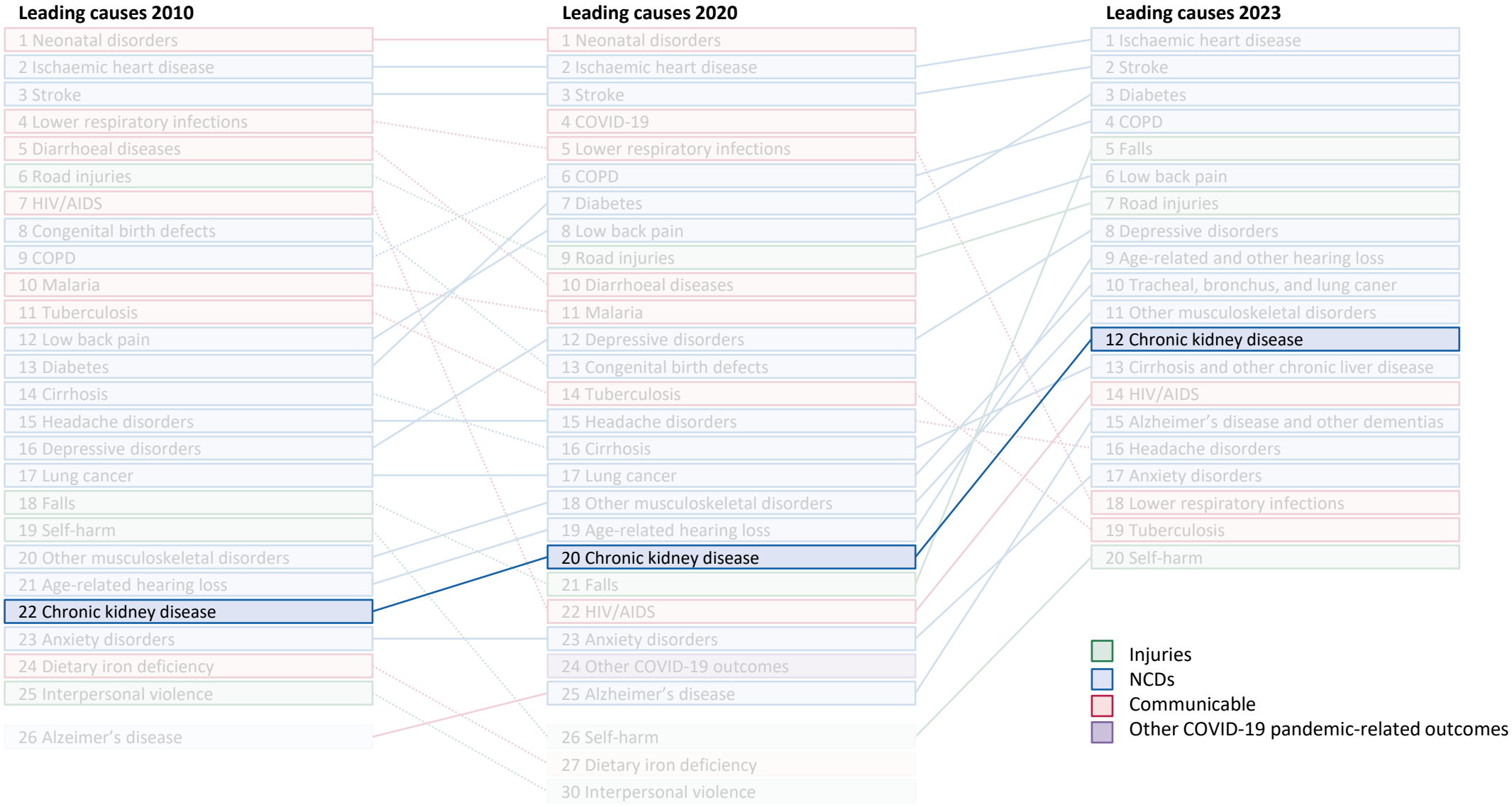


GBD systematically underestimates the burden of CKD on deaths and disability

2023

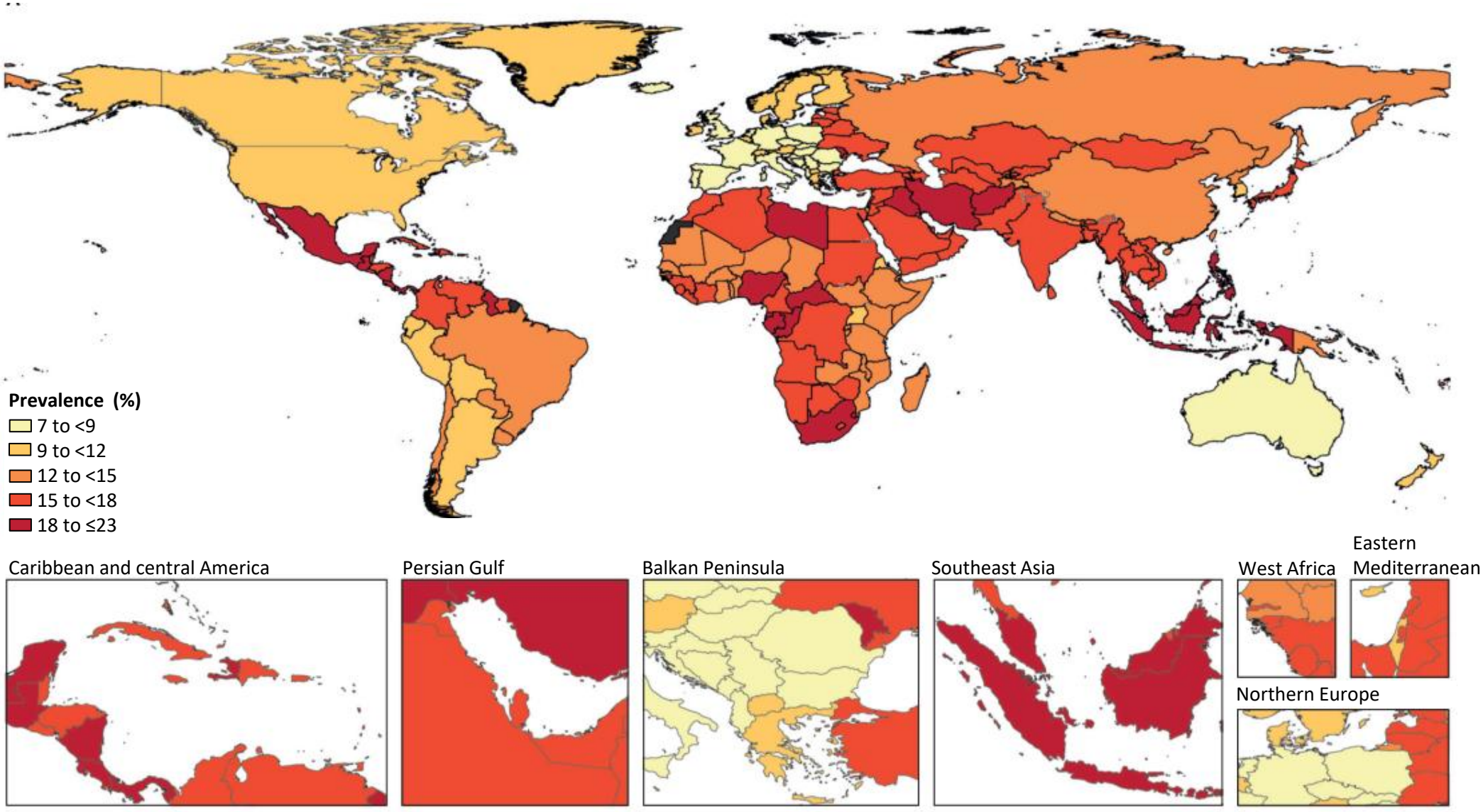
Leading CVD mortality risk factors	Population attributable fraction (%)
1 High systolic blood pressure	55·1 (45·6 to 62·6)
2 Dietary risks	30·8 (12·0 to 44·8)
3 Air pollution	20·7 (16·2 to 25·2)
4 High LDL cholesterol	19·0 (11·8 to 27·6)
5 Other environmental risks	18·0 (14·4 to 21·7)
6 Tobacco	15·3 (13·0 to 17·7)
7 Kidney dysfunction	11·5 (8·4 to 14·5)
8 High fasting plasma glucose	9·9 (8·3 to 12·2)
9 High body-mass index	9·4 (5·5 to 13·3)
10 Non-optimal temperature	6·1 (5·3 to 7·4)
11 Low physical activity	1·9 (0·6 to 3·2)
12 High alcohol use	0·9 (0·2 to 2·2)

Environmental and occupational risks
Behavioural risks
Metabolic risks

Due to the weirdness of GBD methods, these deaths are due to ”kidney dysfunction” but are counted as “cardiovascular deaths”

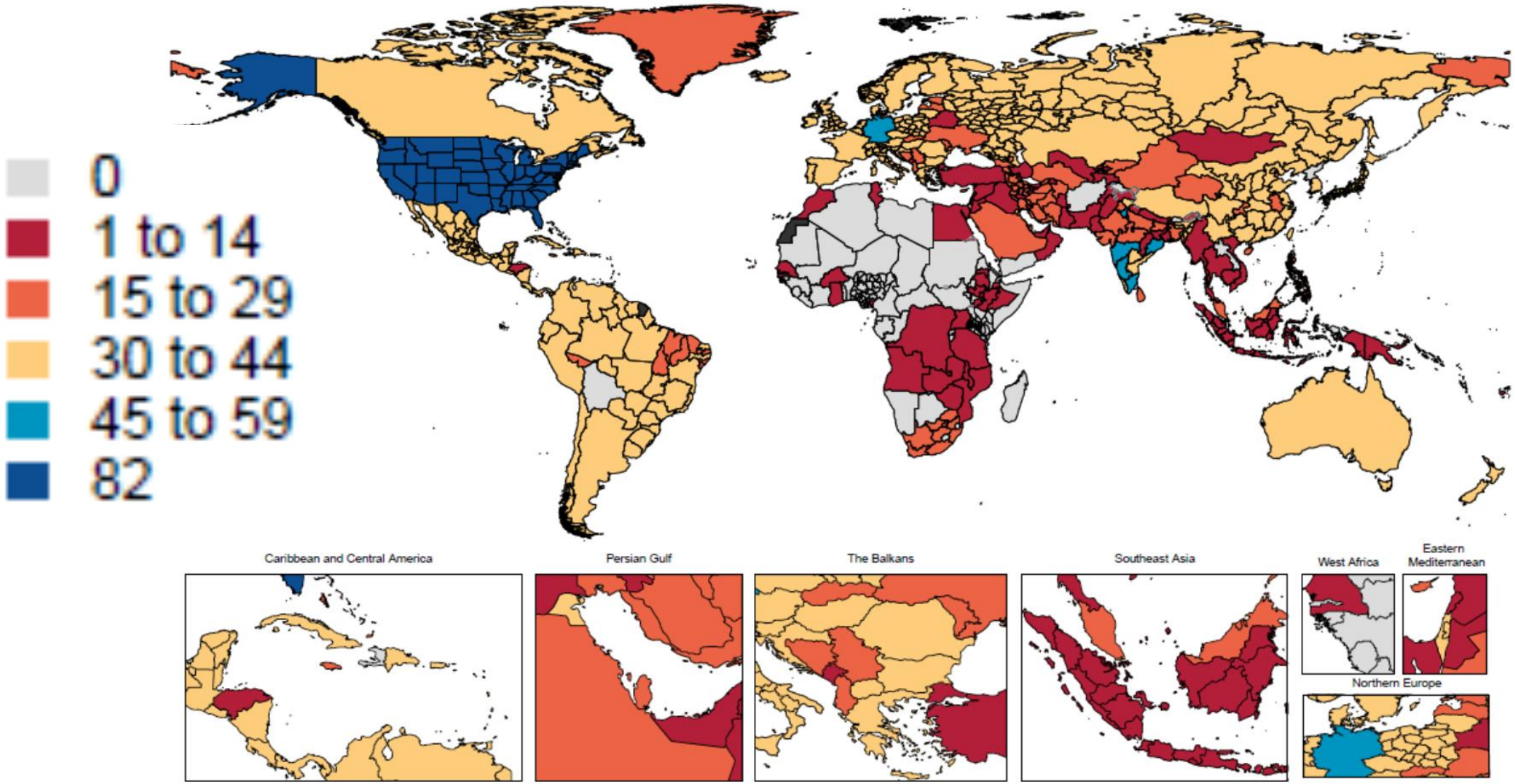
GBD CKD Collaborators. Lancet 2025

CKD affects ~800 million adults



GBD CKD Collaborators. Lancet 2025

But much of the data are missing or very sparse



GBD CKD Collaborators. Lancet 2025

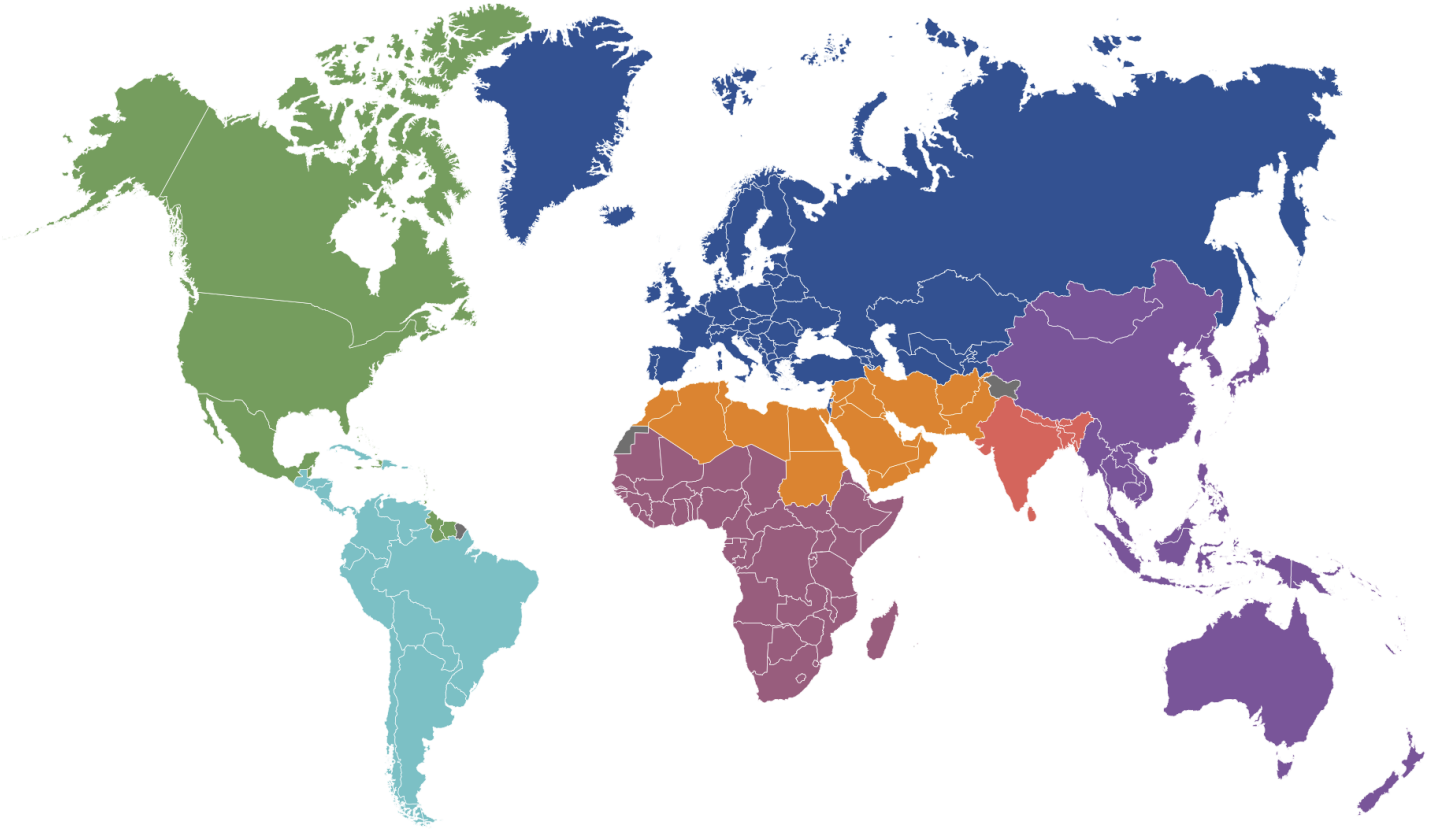
The global number of people with diabetes continues to increase

World	
2045	783 million
2030	643 million
2021	537 million
↑	46% increase

North America & Caribbean (NAC)	
2045	63 million
2030	57 million
2021	51 million
↑	24% increase

Europe (EUR)	
2045	69 million
2030	67 million
2021	61 million
↑	13% increase

Western Pacific (WP)	
2045	260 million
2030	238 million
2021	206 million
↑	27% increase



South & Central America (SACA)	
2045	49 million
2030	40 million
2021	32 million
↑	50% increase

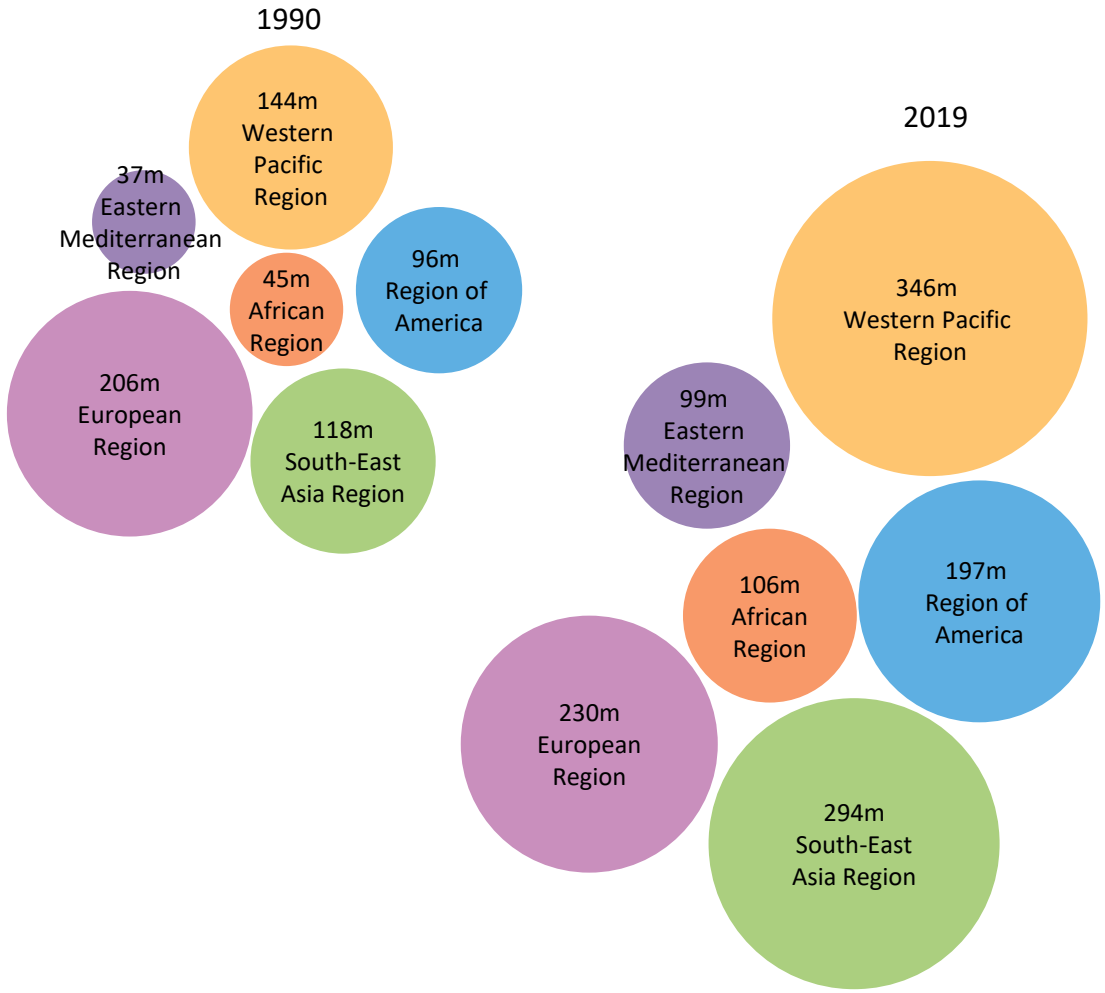
Africa (AFR)	
2045	55 million
2030	33 million
2021	24 million
↑	134% increase

Middle East & North Africa (MENA)	
2045	136 million
2030	95 million
2021	73 million
↑	87% increase

South-East Asia (SEA)	
2045	152 million
2030	113 million
2021	90 million
↑	68% increase

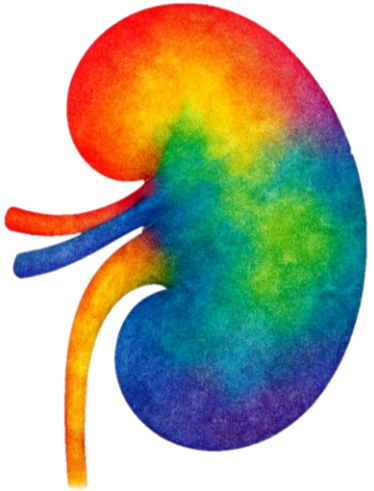
So does the number of people with hypertension

Number of adults with hypertension, 1990 and 2019



IDF Diabetes Atlas, 2021 and WHO Global Report on Hypertension, 2024

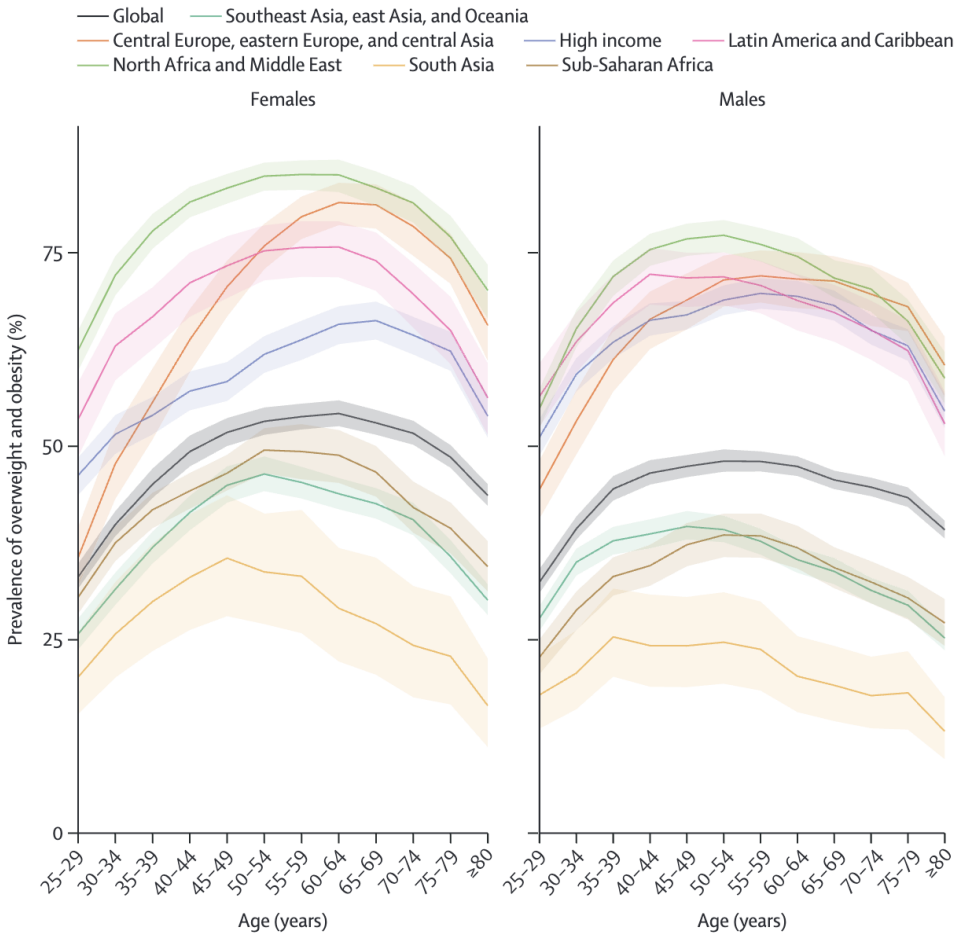
Outline



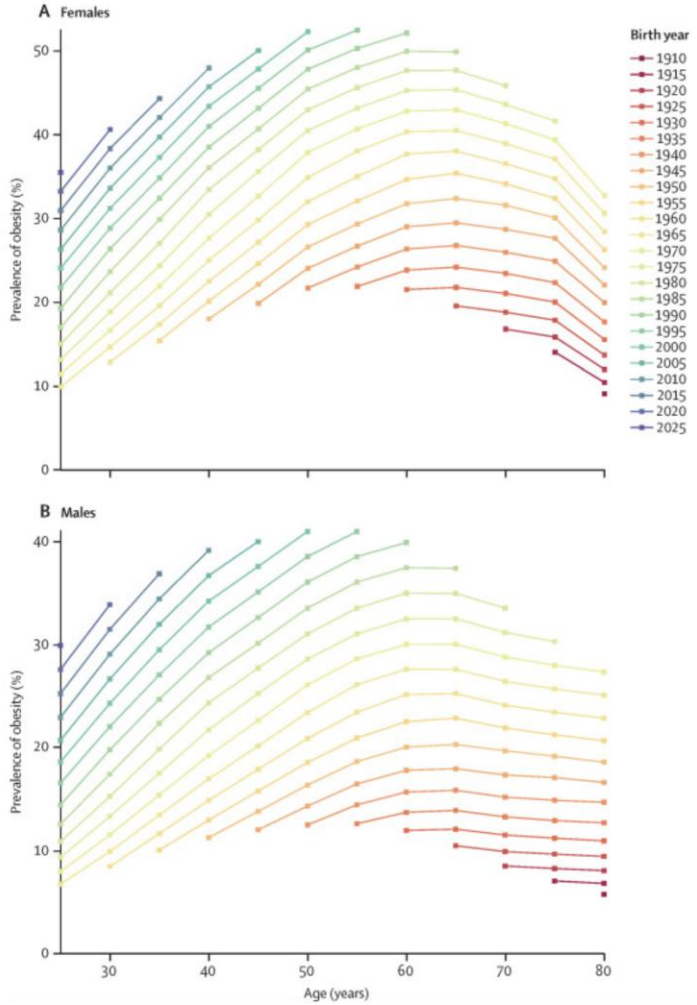
- What is the current and future burden of kidney disease
- How does obesity contribute to the burden of kidney disease?
- Challenges and future directions

The epidemiology of obesity is interesting…& consistent

Prevalence of overweight/obesity by age

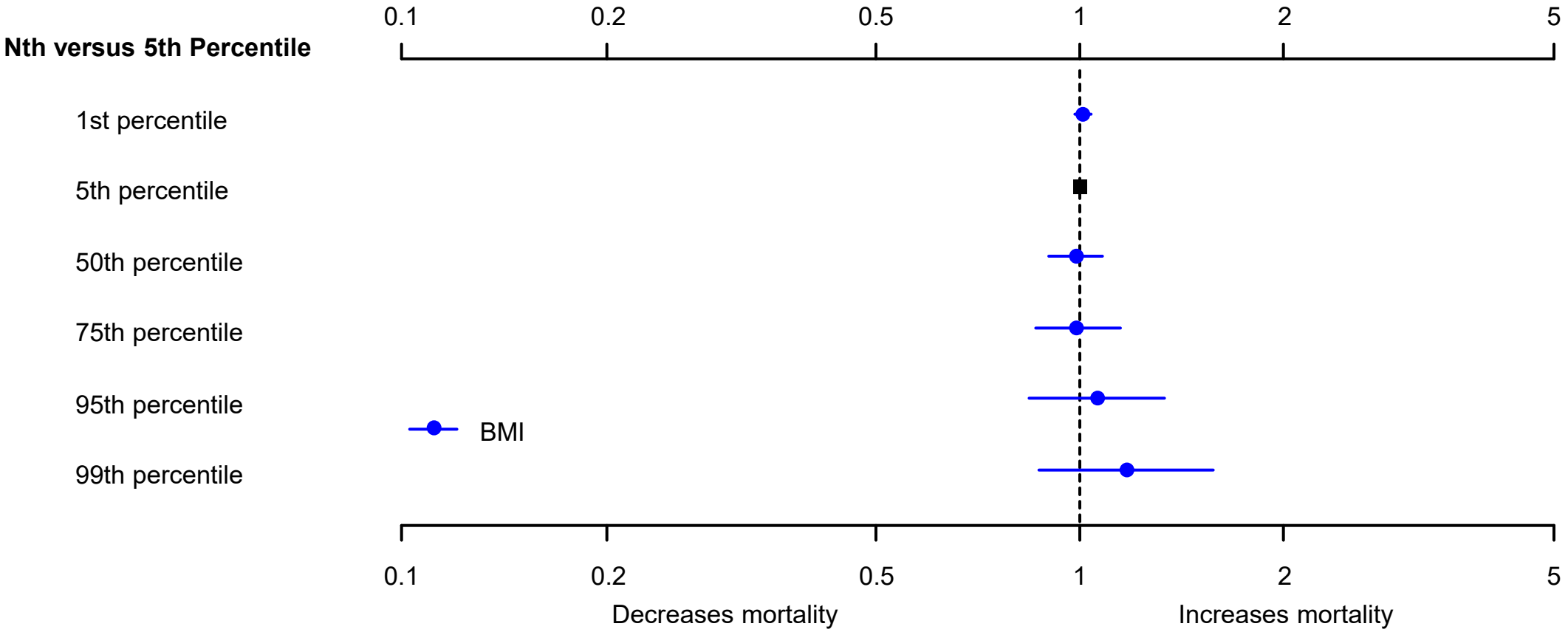


Prevalence of obesity by birth cohort



GBD BMI Collaborators. Lancet 2021

After full adjustment for comorbidity, obesity has a weak association with all-cause mortality

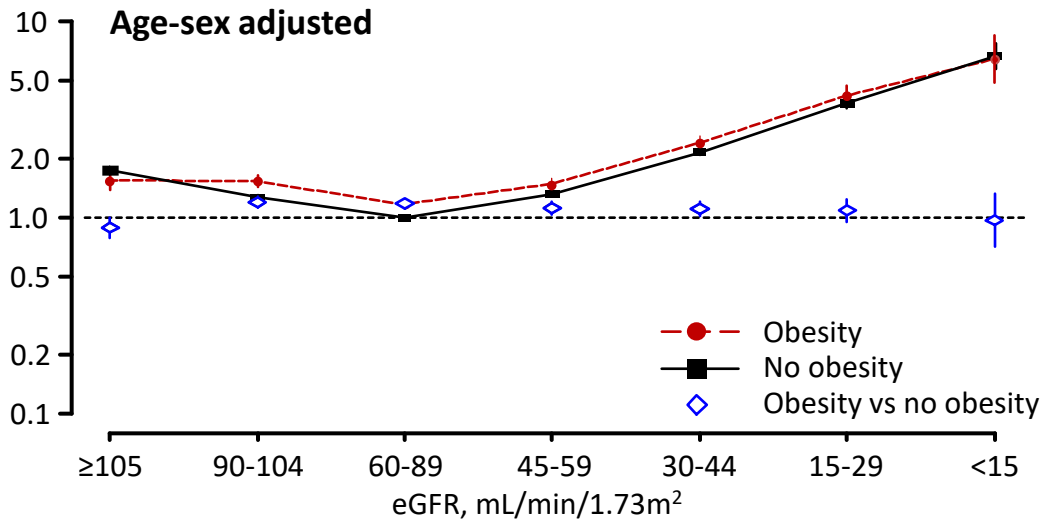


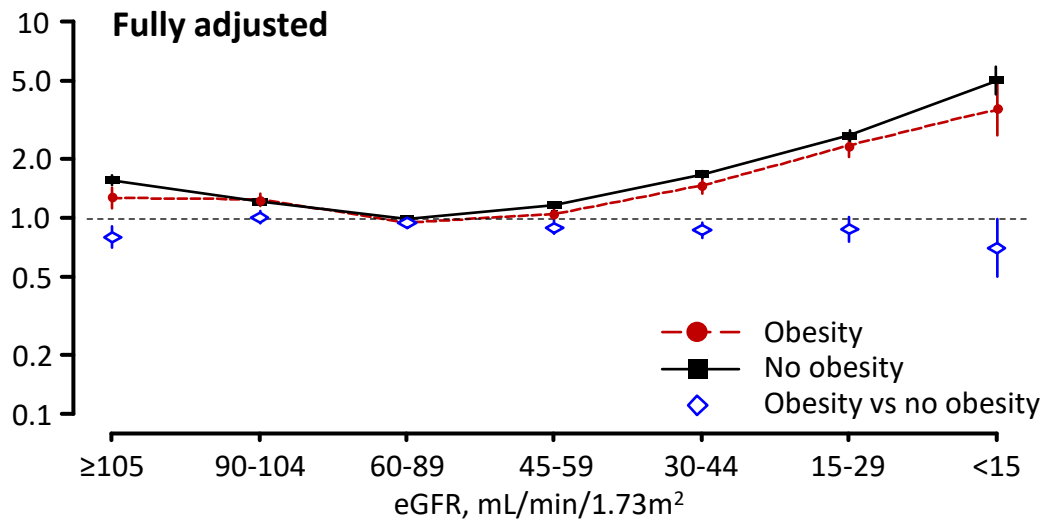
Wiebe et al, Int J Obes 2022

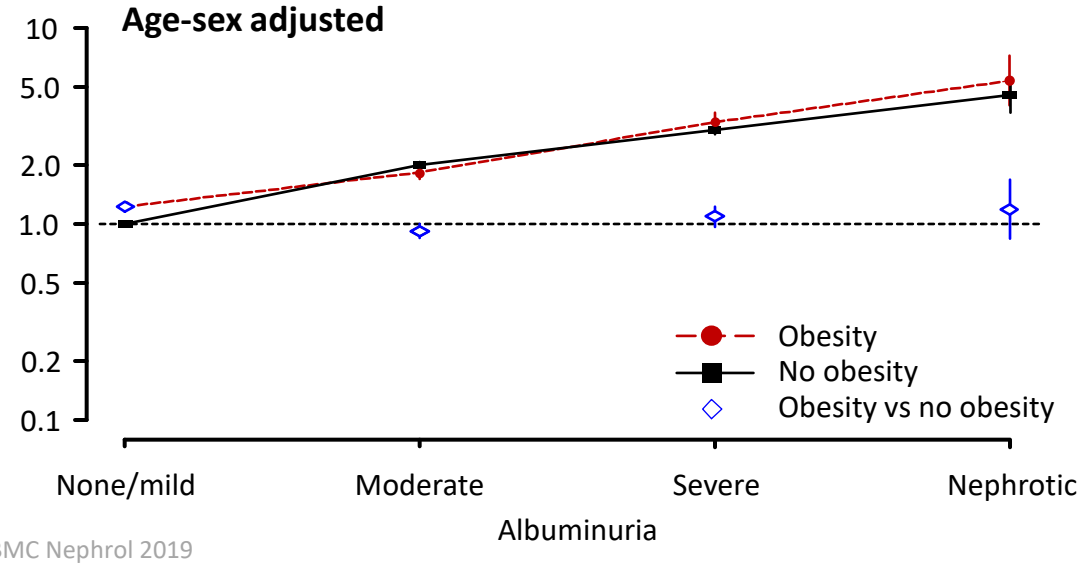
N=8280

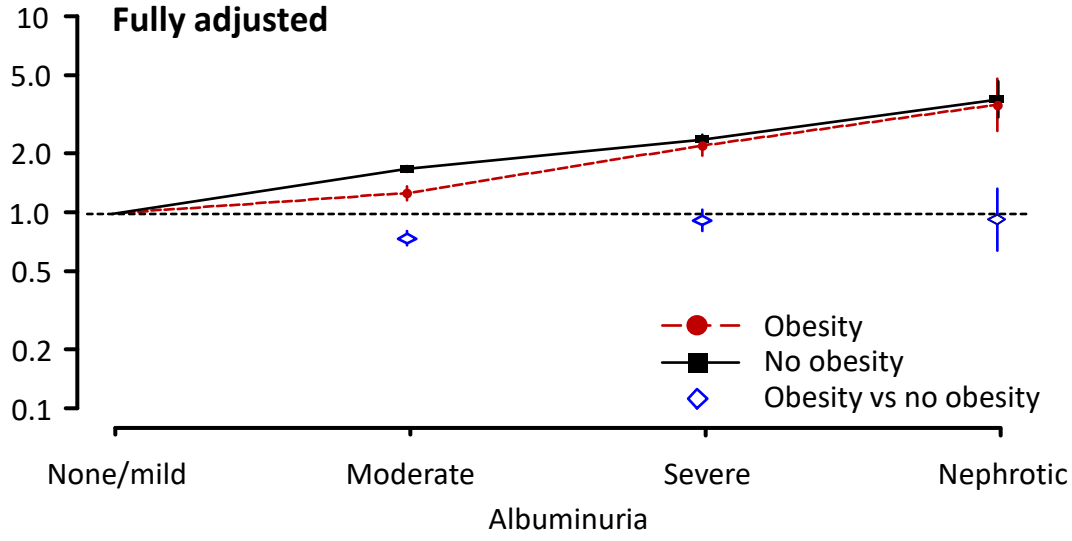
p for interaction between obesity and GFR, 0.008
p for interaction between obesity and albuminuria, 0.001

Not in CKD patients either









Tonelli et al, BMC Nephrol 2019